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PATENT
Attorney Docket No.: 011823-008120US

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By: ______________________

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: G. Ewoldt
Vasquez et al.	Art Unit: 1644
Application No.:	PRELIMINARY AMENDMENT
Filed: November 13, 2001	
For: HUMANIZED ANTIBODIES TO GAMMA-INTERFERON	

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination of the above-referenced application, please enter the following amendments and remarks.

IN THE CLAIMS:

Please cancel claims 1-13.

Please add the following new claims:

14. A humanized immunoglobulin, which is a humanized version of the mouse AF2 immunoglobulin having a light chain variable region designated SEQ ID No:2 and a heavy chain variable region designated SEQ ID No:4, the humanized immunoglobulin comprising humanized heavy and light chains, provided that position 11

according to the Kabat numbering system of the humanized heavy chain variable region framework is occupied by the amino acid present in the equivalent position of the mouse AF2 heavy chain variable region framework.

15. A humanized immunoglobulin, which is a humanized version of the mouse AF2 immunoglobulin having a light chain variable region designated SEQ ID No:2 and a heavy chain variable region designated SEQ ID No:4, the humanized immunoglobulin comprising humanized heavy and light chains, provided that position 11 according to the Kabat numbering system of the humanized heavy chain variable region framework is substituted with the amino acid present in the equivalent position of the mouse AF2 heavy chain variable region framework.

16. The humanized immunoglobulin of claim 15 that specifically binds to human γ-IFN with an affinity constant within four-fold of the affinity of the mouse AF2 antibody.

17. A humanized immunoglobulin that specifically binds to γ-IFN comprising a humanized mature light chain of SEQ ID NO: 6, and a humanized mature heavy chain having at least 90% sequence identity to the mature heavy chain of SEQ ID NO: 8.

18. The humanized immunoglobulin of any of claims 14, 15, 16 or 17, comprising CDRs from the mouse AF2 immunoglobulin and heavy and light chain variable region frameworks from the human EU immunoglobulin.

19. The humanized immunoglobulin of claim 18, further provided that position H38 according to the Kabat numbering system is occupied by the amino acid present in the equivalent position of the mouse AF2 heavy chain variable region framework.

20. The humanized immunoglobulin of claim 18, further provided that positions H11, H27, H28, H30, H38, H48, H67, H68, H70, H72, H74, H93, H95, H98, H107, H108, H109, H111 according to the Kabat numbering system are occupied by the amino acid present in the equivalent position of the mouse AF2 heavy chain, positions L48 and L70 according to the Kabat numbering system are occupied by the amino acid present in the equivalent position of the mouse AF2 light chain, and position L63 is occupied by the amino acid present in the equivalent position of a consensus sequence of light chains of human immunoglobulins.

21. The humanized immunoglobulin according to any of claims 14, 15, 16 or 17 that comprises two light chain/heavy chain dimers.

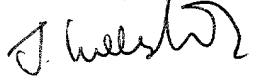
22. The humanized immunoglobulin of any of claims 14, 15, 16 or 17 that is of IgG1 isotype.

23. The humanized immunoglobulin according to any of claims 14, 15, 16 or 17 which is purified to at least 95% homogeneity.

REMARKS

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Vasquez et al.

Application No.: Unassigned

Filed: November 13, 2001

For: HUMANIZED ANTIBODIES TO GAMMA-INTERFERON

Examiner: G. Ewoldt

Art Unit: 1644

PRELIMINARY AMENDMENT

AND

COMMUNICATION UNDER

37 § C.F.R. 1.821-1.825

Box SEQUENCE
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In order to comply with Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, 37 C.F.R. § 1.821-1.825, Applicants submit that the computer readable form in the instant application is identical with the Substitute Sequence Listing filed in Application No. 09/450,520, filed November 29, 1999. In accordance with 37 C.F.R. § 1.821(e), please use the computer readable form filed in that application as the computer readable form for the instant application.

It is understood that the Patent and Trademark Office will make the necessary change in the application number and filing date for the computer readable form that will be used for the instant application. A paper copy of the Sequence Listing is included for incorporation into the Specification.

Please amend the specification in adherence with 37 C.F.R. § 1.821-1.825 as follows:

IN THE SPECIFICATION:

Please replace the paragraph beginning on page 5, line 12, with the following amended paragraph:

Fig. 3 Comparison of the heavy chain variable region amino acid sequence of humanized immunoglobulin HuZAF(SEQ ID NO:10) and humanized immunoglobulins haf25(SEQ ID NO:11), and HuXAF(SEQ ID NO:9).

Please replace the paragraph beginning on page 11, line 3, with the following amended paragraph:

Position H11 does not fulfill the criteria for substitution given above, but nevertheless makes a significant contribution to neutralizing activity in humanized immunoglobulins incorporating this substitution. The desirability of substituting at this position was determined by substitution of various positions in a chimeric AF2 antibody (i.e., having mouse variable domains and human constant regions) with amino acids from equivalent positions in the human EU antibody(SEQ ID NOS:12 and 13). Substitution of position H11 caused a significant reduction in the neutralizing activity of the chimeric antibody for γ-IFN.

Please insert the accompanying paper copy of the sequence listing, page numbers 1-9, at the end of the application.

REMARKS

Applicants request entry of this amendment in adherence with 37 C.F.R. §§ 1.821-1.825. The information contained in the computer readable disk of Application No. 09/450,520 was prepared through use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the specification by the amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning on page 5, line 12, has been amended as follows:

Fig. 3 Comparison of the heavy chain variable region amino acid sequence of [mouse AF2,] humanized immunoglobulin HuZAF(SEQ ID NO:10) and humanized immunoglobulins haf25(SEQ ID NO:11), and HuXAF(SEQ ID NO:9).

The paragraph beginning on page 11, line 3, has been amended as follows:

Position H11 does not fulfill the criteria for substitution given above, but nevertheless makes a significant contribution to neutralizing activity in humanized immunoglobulins incorporating this substitution. The desirability of substituting at this position was determined by substitution of various positions in a chimeric AF2 antibody (i.e., having mouse variable domains and human constant regions) with amino acids from equivalent positions in the human EU antibody (SEQ ID NOS:12 and 13). Substitution of position H11 caused a significant reduction in the neutralizing activity of the chimeric antibody for γ-IFN.